

REMARKS

Enclosed is a \$60 check for the Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050.

Claims 20-22 and 62-82 are pending in this application. Claims 20, 62, 63, 67-71, 73-76 and 78-82 are amended. Applicant acknowledges that the Examiner has renumbered misnumbered claims from the previous amendment. Accordingly, claims 67, 69-71, 73-76 and 78-82 are amended herein to reflect the proper claim dependencies to the claims as renumbered.

Claim 20 is amended to clarify the claimed subject matter by reciting that methylation is reduced as compared to a control plant and that the transcription product comprises a sequence encoding a full length or partial sequence of *Arabidopsis MET1*. Basis for this amendment can be found for example at pages 11-12, and at pages 25-26, including Table 1. Basis can also be found for example at page 10, line 27 to page 11, line 4 and in the claims as originally filed. Claim 21 is amended to correct a typographical error, so that transcription product refers to the antecedent in claim 20. Claim 61 is amended herein to correct an inadvertent grammatical error. Claim 62 is amended to recite a method of production of modified endosperm where the transcription product comprises a full length or partial sequence orthologous to *Arabidopsis MET1*. Claims 63, 69 and 74 dependent thereon further specify species of transcription products. Basis for these amendments can be found, for example, at Examples 3 and 4, pages 30-32 and in the claims as originally filed. Claims 22, 40-61, 68, 70, 75 and 79 are canceled herein without prejudice or disclaimer. Applicant reserves the right to file divisional and/or continuation applications to any of the cancelled subject matter.

I. Claim Objections

As explained above, Applicant acknowledges the Examiner's renumbering of the claims and has amended the claims accordingly to reflect this renumbering.

II. Claim Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 20-22 and 62-82 are rejected under 35 U.S.C. § 112, second paragraph as indefinite. In light of the amendments and remarks herein, reconsideration and withdrawal of the rejection is respectfully requested.

Claim 20

The Office Action alleges that the term “reduces” is indefinite because the term is not defined by the claim, nor a standard in the specification such that one of ordinary skill in the art would be reasonably apprised of the scope of the claimed subject matter.

Applicant respectfully submits that the standard for reduced methylation is in comparison to a control plant as evidenced by the use of the term in the instant application and the use of the term in the art. For further clarity, however, the instant claim is amended to recite a comparison to a control plant. Applicant respectfully submits that the term “reduces” is a well-known term such that one of skill in the art would recognize the metes and bounds of the claimed subject matter. The instant specification and claims use the term “reduces” in reference to methylation and other plant phenotypes in a context that would be understood by one of skill in the art to refer to a comparison between the modified plant and a control plant (see for example, at pages 11-12, points 1-4 describing comparisons of *MET1*.as plants and *ddm* plants in comparison to control plants and at pages 25-26 “Crosses involving *Met1*as Plants,” especially Table 1 and its description comparing the modified plants to control plants).

Additionally, the use of the term “reduced” and “reduces” throughout the application is consistent with the use of the term in the art. The instant application references Ronemus *et al.* (Science 273: 654-57 (1996)) as well as Finnegan *et al.* (Proc. Natl. Acad. Sci. 93: 8449-54 (1996)), both of which use the term “reduces” and “reduction” of methylation in comparison to control plants. For example, Ronemus *et al.* describe *ddm* mutants as having “reduced levels of cytosine methylation” (page 654, column 1). Table 1 of Ronemus *et al.* present a comparison of methylation in *ddm* mutants as compared to wildtype control plants. This data is further explained on page 655, describing the *ddm* plants as having a “reduction” in methylation. Finnegan *et al.* explain that plants transformed with *MET1*. antisense are compared with control plants (page 8450, col. 2) and show the reduction in methylation as compared to control plants (for example, Tables 1-3, page 8450).

Claims 22, 62-63, 69-70, and 74-75

It is alleged that claims 22, 62-63, 69-70, and 74-75 are indefinite in the recitation of “*MET1*,” because the term is arbitrary and creates ambiguity in the claims. Although claim 22 is canceled herein, the limitations of claim 22 are incorporated into claim 20 as amended herein. Hence, this rejection is addressed as it pertains to the instant claims, including claim 20.

An Applicant can be his or her own lexicographer [see, e.g., MPEP 2111.01 “Applicant may be his or her own lexicographer as long as the meaning assigned to the term is not repugnant to the term's well known usage and utilize terms within the claims that are clear from a reading of the specification. *In re Hill*, 73 USPQ 482 (CCPA 1947)"]. The instant specification describes *MET1* as a methylation enzyme from *Arabidopsis* (page 10, line 27 to page 11, line 4). The specification references Finnegan *et al.* and Ronemus *et al.* for the *MET1* gene (page 10, line 29). These articles both explain that *MET1* refers to the *Arabidopsis* cytosine methyltransferase gene that was published in 1993 under the Genbank number L10692 (see references cited within both articles, pointing to Finnegan *et al.* (1993) Nuc. Acid Res. 21:2383-2388). In addition, Figure 6 of the instant application depicts the *MET1* gene including the hybridization of the primer sequences presented on page 27, SEQ ID NOS: 5 and 6. These primer sequences identify the *MET1* gene. For example, a BlastN search using these primers identifies the *MET1* Genbank entry L10692, the same Genbank reference pointed to by Finnegan *et al.* and Ronemus *et al.* Therefore, Applicant respectfully submits that one of skill in the art would recognize the metes and bounds of the claimed subject matter based on the use of the term “*Arabidopsis MET1*” as used in the instant application and as set forth in the instant claims.

III. Claim Rejections under 35 U.S.C. § 112, Written Description

Claims 20-22 and 62-82 are rejected under 35 U.S.C. § 112, first paragraph as containing subject matter that was not described in the application in such a way as to convey to one skilled in the relevant art that the inventors had possession of the claimed subject matter at the time the application was filed. In particular, it is alleged that the Applicant has not provided a nucleic acid molecule encoding *Arabidopsis MET1*, nor a correlation between nucleic acid structure and function. It is further alleged that no additional *MET1* sequences such as *Z. mays* or *B. napus* orthologs or ribozyme sequences are disclosed. The Office

Action concludes that because the Application does not identify any specific structural features of the genus, nor necessary essential elements for the *MET1* protein, the specification fails to provide an adequate written description to support the breadth of the claims.

Applicant respectfully request reconsideration and withdrawal of the rejection.

Analysis

An objective standard for determining compliance with the written description requirement is "does the description clearly allow persons of skill in the art to recognize that he or she invented what is claimed." In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ.2d 1614, 1618 (Fed. Cir. 1989). Thus, the knowledge and level of skill in the particular art is a factor to be considered in determining the standard.

The instant claims are drawn to the production of modified endosperm by reducing methylation. The methods include directing expression of *Arabidopsis MET1* in female germ line tissue of a plant. Dependent claims are also drawn to expression of *Z. mays* Met 1 orthologs, antisense, sense and partial sense copies and ribozymes of *Arabidopsis* and *Z. mays MET1*. The application describes each step of the claimed methods in sufficient detail to convey to one of skill in the art that the Applicant was in possession of the claimed subject matter at the time of filing. Such disclosures include a description of DNA methylation enzymes in *Arabidopsis* and other organisms and regulatory sequences capable of directing expression in female germ line tissues.

Arabidopsis MET1

The instant application identifies *Arabidopsis MET1* as an *Arabidopsis* gene with a known sequence as evidenced by the published literature (see for example, at page 10, line 27 to page 11, line 4, referencing Finnegan *et al.* and Ronemus *et al.*). In addition, Figure 6 of the application schematically describes the structure of Met 1. Primer sequences that amplify *MET1*, Met1F and Met1R (SEQ ID NOS:5 and 6), are presented in the application at page 30. The locations of these primer sequences in *MET1* are identified in Figure 6. Each of these descriptions is sufficient to identify *Arabidopsis MET1* to one of skill in the art.

Additionally, the application provides Genbank numbers for a number of additional methylating enzymes (pages 18 and 19). *Arabidopsis MET1* is included among this list; however an inadvertent typographical error was made. Accession number C10692 is incorrect and should be listed as "L10692." This typographical error would be apparent and

easily rectified by one of skill in the art for the following reasons: (1) the incorrect number identifies an unrelated non-*Arabidopsis* gene; (2) the correct Accession number was known in the art before the time of filing (see Genbank Accession L10692, provided herein); (3) the references in the instant application that describe *MET1* point one of skill in the art to the correct accession number; (4) the primer sequences can be used by one of skill in the art to retrieve the correct accession number using standard sequence alignment programs available in the art at the time of filing. Hence, the application also describes *MET1* by directing one of skill to the Genbank Accession for the *Arabidopsis* gene.

MET1 orthologs

The application additionally describes orthologs of *MET1* that can be used in the methods therein, including *Z. mays* orthologs of Met 1 (see for example, at page 28, lines 8-11). The *Z. mays* *MET1* was known in the art at least since 1998 (see Genbank Accession No. AF063403, provided herein). The Genbank reference describes this accession as a *Zea mays* cytosine-5 DNA methyltransferase (ZMET1) and provides DNA and protein sequence. Hence, the application need not provide any additional description for one of skill in the art to recognize *Z. mays* *MET1* and its use in the instantly claimed methods. Claims directed to *B. napus* *MET1* are cancelled herein without prejudice or disclaimer; hence, with respect to claims encompassing *B. napus* *MET1*, the rejection is rendered moot.

Nucleic Acid Molecules

The specification describes a wide variety of nucleic acid molecules that can be used in the methods to reduce the degree of methylation in a plant. The specification describes, for example, antisense constructs, sense nucleic acids, partial sense nucleic acids and ribozymes. Each of these types of nucleic acids is derived from the sequence of *MET1*. As explained above, *MET1* and its orthologs were available in the art at and before the time of filing of the instant application. The specification also presents nucleic acid molecules containing *MET1* and *MET1* antisense sequences. Moreover, the types of nucleic acids, e.g. antisense, sense, partial, sense, ribozymes, their design and methods for their generation were well known to one of skill in the art. Hence, one of skill in the art given *MET1*, a known sequence, and the knowledge in the art would understand the Applicant to be in possession of all such types of nucleic acids as they pertain to *MET1*.

The Office Action alleges that ribozymes in particular are not sufficiently described by the instant application. As of the filing date of the instant application, ribozymes were well known nucleic acid molecules for use in plants and other organisms. Ribozymes, like antisense constructs, rely on sequences that are complementary to a gene sequence (see for example, Merlo *et al.* (1998) *Plant Cell* 10:1603-21, provided herein). Thus, one of skill in the art would have recognized that the instant application, which describes ribozymes of *MET1*, encompasses ribozyme structures that are complementary to the known *MET1* sequence. Hence, the *MET1* sequence known in the art at the time of filing and described in the application is sufficient to describe ribozymes that include *MET1* sequences.

In summary, Applicant has described each step of the methods and the nucleic acid molecules used in the methods for one of skill in the art to recognize that Applicant was in possession of the instantly claimed methods. Therefore, Applicant respectfully requests withdrawal of the rejection.

IV. Claim Rejections under 35 U.S.C. § 112, Enablement

Claims 20-22 and 62-82 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabled for a method that includes a construct comprising the *MET1* cDNA operable linked to any promoter expressed in male or female gametophyte in antisense orientation and plants transformed therewith, does not enable claims more broadly drawn. In particular, it is alleged that the methods of modifying endosperm are not enabled using any nucleic acid sequence, including any Met 1 such as *Z. mays* or *B. napus* Met orthologs, partial or full length sense copies or ribozymes of *MET1*. It is further alleged that the references cited in the Office Action, including Fourgoux-Nicol *et al.* (1999, *Plant Mol. Biol.* 40:857-72), Gutterson (1995, *HortScience* 30(5):964-66), Emery *et al.* (2003, *Current Biology* 13: 1768-74), Mazzolini *et al.* (1992, *Plant Mol. Biol.* 20:715-31), evidence the unpredictability of techniques such as nucleic acid hybridization, sense suppression, micro-RNA pairing and ribozymes. The Office Action therefore concludes that it would require undue experimentation to practice the methods as claimed.

This rejection is respectfully traversed.

ANALYSIS

The inquiry with respect to scope of enablement under 35 U.S.C. §112, first paragraph, is whether it would require undue experimentation to make and use the claimed

invention. A considerable amount of experimentation is permissible, particularly if it is routine experimentation. The amount of experimentation that is permissible depends upon a number of factors, which include: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability of the art, and the breadth of the claims. Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int'l 1986); see also In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). A consideration of these factors demonstrates that the application, in conjunction with what was known to one of skill in the art, teaches how to make and use the full scope of the claimed subject matter. It would not require undue experimentation to practice the instantly claimed methods of producing modified endosperm using a nucleic acid molecule that includes one or more regulatory sequences directing expression in female germ line cells and a sequence whose transcription product comprises a full-length or partial *Arabidopsis MET1* sequence or a *Z. mays* ortholog.

The scope of the claims: The claims are directed to methods of modifying endosperm by introducing a nucleic acid molecule that includes one or more regulatory sequences directing expression in female germ line cells and a sequence whose transcription product comprises a full-length or partial *MET1* sequence. The introduced DNA is effective for down-regulating one or more DNA methylating enzymes present in the plant, whereby the degree of DNA methylation of nucleic acid in the plant is reduced as compared to a control plant. Claim 20 and claims dependent thereon are directed to *Arabidopsis MET1* sequences. Claim 62 and claims dependent thereon are directed to methods where the transcription product comprises a *Z. mays* sequence orthologous to *Arabidopsis MET1*. Transcription products used in the methods can include antisense molecules, sense and partial sense copies or ribozymes.

The level of skill in this art and knowledge of those of skill in the art is recognized to be high. The numerous articles and patents made of record in this application address a highly skilled audience and further evidence the high level of skill in this art. The cited references evidence the knowledge in the art pertaining to DNA methylation in plants, methylating enzymes in plants and animals and plant promoters, including promoters that direct expression in specific tissues (see e.g., pages 41-47). In addition, the references

evidence the high level of knowledge in that art with respect to plant transformation, endosperm and seed development and phenotypes.

The teachings of the specification provide all of the necessary guidance for one of skill in the art to make and use the claimed methods for modifying endosperm. First, the specification teaches that methylating enzymes such as *Arabidopsis MET1* and *MET1* orthologs can be used to reduce the degree of methylation in a plant (see, for example, at page 18, lines 27-29 and at page 32, lines 6-8). The specification provides exemplary methylase genes (see for example, at page 10, line 27 to 29). In addition, it teaches that such sequences can be used to construct antisense molecules, sense and partial sense molecules and ribozymes (see for example, page 18, line 27 to page 19, line 2). The specification teaches that these sequences can be operably linked to promoters that direct expression in female germ line tissue (page 16, lines 8-15). The specification provides numerous exemplary promoters for such expression (see, for example, at page 16, lines 17-25). In addition, the specification provides detailed description of the characteristics of promoter expression that can be used with the methods (page 16, lines 25-28). The specification teaches the assessment of endosperm characteristics including size, weight, cell number and morphology (see for example, at page 25-26 and Figures 1-3 and 8-12).

Working Examples are provided that exemplify the claimed methods. Example 2 details the construction of germ line expression vectors. Example 3 exemplifies the construction of *MET1* antisense with germ line promoters. This example also teaches that sense, partial sense and ribozymes expression constructs can be produced for similar germ line expression. Example 4 exemplifies transformation of germ line specific *MET1* constructs into *Arabidopsis*, and additionally teaches that transgenic plants can be made following similar methods with *MET1* orthologs including *Z. mays MET1*. Example 5 includes transformation of *MET1* constructs into additional plants such as *Brassicas* and assessment of endosperm phenotypes in interspecific crosses. Examples 6-9 detail further characterizations of *MET1* constructs and endosperms of plants transformed with such constructs in different plant backgrounds.

Predictability: In contrast to the Office Action's allegation of unpredictability of the art, the art of down-regulating genes was well-established and routine as of the time of filing of the instant application. Antisense down-regulation, sense suppression and the use of

ribozymes for down-regulating genes were all well established techniques in the art (see e.g., references discussed below). Moreover, the instant application demonstrates that using the claimed methods, the expression of a *MET1* antisense construct in female germ line tissue results in modified endosperm. The application further teaches that other methods of down-regulation can be used to achieve the same result. In addition, the application explains that orthologs of *MET1* can be used to produce modified endosperm.

The Office Action alleges that Jacobsen *et al.* (2003, Curr. Biol. 10:179-86) teach the unpredictability of the art because the transformation of *Arabidopsis* with *MET1* antisense which causes a decrease in methylation by 80-90% also hypermethylates and silences the Superman gene. Applicant respectfully disagrees. First, the Superman gene and floral morphology, the subject matter of Jacobsen *et al.*, are not the subject matter of the instant claims. Instead, the claimed methods are directed to modified endosperm, a phenotype which Jacobsen *et al.* do not address. The Examiner has provided no connection between the Superman gene or floral phenotype and the effect of reduced methylation on modified endosperm. Second, Jacobsen *et al.* do not assert that antisense is unpredictable, nor that the *MET1* gene is unpredictable. The working examples in the instant application, *e.g.*, Examples 1-5, are consistent with the predictability of antisense technology, demonstrating that the claimed methods are operable in different genetic conditions. The Examiner has provided no basis on which to doubt the veracity of the teachings of the application.

The Office Action also alleges that because the application provides only primers for *Arabidopsis MET1*, applicant has not disclosed how one makes or isolates any of the other sequences that are encompassed by the broad claims. Applicant respectfully disagrees. “A patent need not teach and preferably omits what is well-known in the art.” MPEP §2164.01 (quoting *In re Buchner* 929 F.2d 600, 661 (Fed. Cir. 1986)). One of skill in the art was very familiar with cloning by hybridization and PCR methods orthologs of genes (*see e.g.*, Gutterson *et al.* 1995, Hort Sci. 30 at page 965. col. 2). Moreover, as explained above, the *Z. mays MET1* was known in the art at the time of filing. Hence, using any of the numerous techniques available, one of skill in the art could make *MET1* constructs from any species, including *Z. mays*.

The Office Action further contends that Fourgoux-Nicol *et al.* (1999, Plant Mol. Biol. 40:857-72) teach that DNA fragments do not always hybridize with the expected

complementary DNA. Further, it is alleged that this reference demonstrates that degenerate primers do not always produce the expected results. In contrast to the characterization of this reference as teaching “unpredictability,” Applicant respectfully submits that this reference demonstrates that one of skill in the art can isolate related gene sequences *even if* their DNA sequences do not completely match. First, the authors of the Fourgoux-Nicol reference show that using a partial cDNA clone, additional cDNA clones and genomic clones can be isolated using routine hybridization methods. The clones isolated were all related genes from a gene family, a phenomena well-known and recognized in the art. Second, the reference has no mention of degenerate primers, nor would such reference be pertinent to the instant issue. Although degenerate PCR is one method of isolating orthologs, there were many established methods that one of skill in the art could use. Applicant’s method is not limited to any particular method of isolating such orthologs.

The Office Action also cites Gutterson *et al.* (1995, Hort Sci. 30:964-66) as allegedly teaching unpredictable results of co-suppression. It is alleged that the reference teaches that transforming a petunia plant with a chrysanthemum CHS gene did not result in suppression of the endogenous CHS gene. First, the reference demonstrates that genes with at least 85% sequence identity can be employed for co-suppression (page 965, 2nd column). Second, the reference demonstrates that where species exhibit additional sequence diversity, one of skill in the art had additional methods to achieve sense suppression, for example, the use of small fragments with identity between the genes (*e.g.*, as small as 225 bp; page 965, col. 2) and the isolation and use of the orthologs (page 967). Third, the instant application demonstrates that for *MET1*, cross-species hybridization is an effective strategy for down-regulation. Example 5 demonstrates that an *Arabidopsis MET1* antisense transformed into *Brassica campestris* and *Brassica oleraceae* could overcome the normal barrier to interspecific hybridization. Hence, with respect to the instantly claimed subject matter, the down-regulation of *MET1*, inter-species down-regulation has been demonstrated and it is not “unpredictable.”

Emery *et al.* (2003, Current Biol. 13: 1768-1774) is cited as allegedly describing experiments that demonstrate altered base-pair micro-RNAs do not bind to a target sequence and that such data evidences that antisense molecules exhibiting less than 100% identity to the target sequence produce unexpected results. First, this reference was published after the filing date of the instant application. Enablement is assessed as of the priority date, and post

filings-date references can only be used “if individuals of skill in the art state that a particular invention is not possible years after the filing date....”MPEP §2164.05(a). Emery *et al.* do not describe the state of the art as of the filing date of the instant application, nor that a particular technique relevant to the instant claims was not possible as of or after the filing date of the instant application. Moreover, regardless of the publication date of Emery *et al.*, this reference provides no evidence whatsoever of “unpredictability” of the art with respect to the down-regulation of methylase genes in plants. The passage cited by the Examiner (page 1769, 2nd column) refers to an experiment to determine if the gain of function phenotype of REV was produced by the loss of hybridization with an endogenous micro-RNA. The authors purposely make a change in the nucleotide sequence that they expect to interfere with binding to the cDNA; the authors achieve the predicted result. Hence, the results demonstrate the predictability of the art, not its unpredictability. Moreover, it should be noted that micro-RNAs are about 21-26 nucleotides in length. The hybridization properties of a micro-RNA have little or no bearing on antisense regulation which generally uses much larger nucleic acid molecules (see for example, Jacobsen *et al.*).

Lastly, the Office Action cites Mazzolini *et al.* (1992, Plant Mol. Bio. 20: 715-31) as demonstrating the unpredictability of using ribozymes to down-regulate a particular gene, because the paper states that the lowered gene expression was not found to be statistically significant. First, Applicant respectfully points out that this reference was published 7 years before the instant Application’s earliest filing date (1999). Hence, it does not represent the state of the art at the time of filing. By 1999 the state of the art of ribozyme technology in plants had reached a more advanced stage. For example, Merlo *et al.* (1998) Plant Cell 10: 1603-21 demonstrate the ribozymes can down-regulate endogenous stearoyl-acyl carrier protein ($\Delta 9$) desaturase genes when transformed into maize. Additionally Yang *et al.* (1997) Proc. Natl. Acad. Sci. 94:4861-65 use hammerhead ribozymes transformed into potato to down regulate potato spindle tuner viroid. The authors achieve complete suppression *in planta*. Hence, as of the earliest filing date of the instant application, ribozymes were a well-established and predictable technology for down-regulating gene expression in plants.

V. Claim Rejections under 35 U.S.C. § 102

Claims 20-22, 64-65, 77-79 and 81 are rejected under 35 U.S.C. § 102(b) as anticipated by Ronemus *et al.* (1996, *Science* 273:654-57). In particular, it is alleged that Ronemus *et al.* disclose an antisense construct comprising *Arabidopsis MET1* in an antisense orientation operably linked to the CaMV promoter and plants transformed with this construct. It is further alleged that Ronemus *et al.* disclose that the transformed plants have substantial demethylation. The Office Action therefore concludes that the publication inherently anticipates the instant claims because the method steps are the same as the Applicant's, the 35S promoter is constitutive and would therefore express in the male and female gametes allegedly resulting in modified endosperm. This rejection is respectfully traversed.

The claims

Claim 20 is directed to a method for producing modified endosperm by introducing a nucleic acid molecule containing one or more regulatory sequences directing expression in female germ line cells and a sequence whose transcription product comprises a full-length or partial *Arabidopsis MET1* sequence. The introduced DNA is effective for down-regulating one or more DNA methylating enzymes present in the plant, whereby the degree of DNA methylation of nucleic acid in the plant is reduced as compared to a control plant. Dependent claims 21, 64-65, 77-79 and 81 incorporate the limitations of claim 20 and additionally specify, for example, the use of antisense, sense or partial sense nucleic acids and *MET1*, directing expression in female gametic cells and the introduction of nucleic acids into dicotyledenous plants.

Differences between the disclosure of Ronemus *et al.* and the rejected claims

The cited reference discloses an *Arabidopsis* Met 1 antisense construct consisting of a full-length *MET1* cDNA in an antisense orientation under the control of a 35CaMV promoter, described therein as a constitutive viral promoter. Ronemus *et al.* also disclose transformation of *Arabidopsis* with this antisense construct. The plants exhibit reduced DNA methylation. Additionally, the transformed plants exhibited developmental abnormalities including secondary branches, vegetative rosettes and gross abnormalities in apical flowers.

Ronemus *et al.* do not disclose any methods of producing modified endosperm. The reference does not disclose any endosperm phenotypes therein. Further, Ronemus *et al.* do not disclose any nucleic acid constructs that direct expression in female germ line cells.

Ronemus *et al.* do not anticipate the instantly claimed methods

Anticipation requires the disclosure in a single prior art reference of each element of the claim under consideration. In re Spada, 15 USPQ2d 1655 (Fed. Cir, 1990), In re Bond, 15 USPQ 1566 (Fed. Cir. 1990), Soundscriber Corp. v. U.S., 360 F.2d 954, 148 USPQ 298, 301, adopted 149 USPQ 640 (Ct. Cl.) 1966. See, also, Richardson v. Suzuki Motor Co., 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir.), cert. denied, 110 S.Ct. 154 (1989). "[A]ll limitations in the claims must be found in the reference, since the claims measure the invention." In re Lang, 644 F.2d 856, 862, 209 USPQ 288, 293 (CCPA 1981).

Ronemus *et al.* do not anticipate the instant claims because they do not disclose each element of the claimed methods. The instant methods include the step of directing expression of *MET1* in female germ line cells. Ronemus *et al.* do not disclose this step. As explained in the instant application, directing expression in female germ line cells leads to the restriction of imprint removal or attenuation in one or other of the gametes (page 15, lines 12-13). Furthermore, the application states that direction of expression to specific tissues is important: "The important property of the nucleic acid molecules used in the transformation step is that DNA of cells that contribute to one sex of germ line is subject to alteration of the pattern of DNA methylation through the activity of the transgenes" (page 15, lines 28-30). The application specifically differentiates directing expression in female germ line cells from the generalized hypomethylation that occurs with a 35SCaMV regulated *MET1* antisense construct (page 15, lines 19-20). Thus, the application explains that the term "directing expression in female germ line cells" relates to the restricted expression in female germ line cells, not generalized expression in other cells such as the other (male) gamete tissue. Nowhere in Ronemus *et al.* is there any mention of such directed expression. Ronemus *et al.* only disclose constitutive expression throughout the *Arabidopsis* plant.

Additionally, although the Office Action alleges that Ronemus *et al.* inherently anticipate the instantly claimed subject matter, Applicant respectfully submits that it does not. An inherent property has to necessarily flow from what is taught in a reference. In re Oelrich, 666 F.2d 578, 581, 212 USPQ 323, 326 (CCPA 1981). Ronemus *et al.* only disclose generalized expression of an antisense *MET1* throughout the plant. Such generalized expression does not inherently direct expression to the female germ line tissue without expression elsewhere in the plant. Moreover, although the Examiner alleges that the methods

disclosed by Ronemus *et al.* would produce the same effect as the instantly claimed methods, no reasoning for such an allegation is provided. Ronemus *et al.* do not mention modified endosperm, nor any modified endosperm phenotypes at all. Furthermore, even if *en arguendo* Ronemus *et al.* were to show production of modified endosperm using the generalized non-directed expression with the CaMV35S promoter (and Applicant respectfully notes that Ronemus *et al.* disclose no such phenotypes), such a showing would not anticipate the instantly claimed subject matter. As noted above, an anticipating reference must disclose each and every step of the claimed method. Ronemus *et al.* do not disclose a method that includes the step of directing expression in female germ line tissue as described in the instant application. Therefore, since Ronemus *et al.* do not disclose each and every step of the method set forth in claim 20, it does not anticipate claim 20 or any of the claims dependent thereon, including claims 21, 64-65, 77-79 and 81 named in this rejection.

* * *

In view of the above, reconsideration and allowance are respectfully requested

Respectfully submitted,



Erica J. Pascal
Reg. No. 47,846

Date: February 25, 2004

Customer No: 26191
Fish & Richardson P.C., P.A.
60 South Sixth Street
Suite 3300
Minneapolis, MN 55402
Telephone: (612) 335-5070
Facsimile: (612) 288-9696